

Amendments to the Claims:

This listing of claims replaces all prior versions and listings of claims in the application:

Listing of Claims:

1. (Currently amended) A screening method comprising:

(a) providing a first plurality of bacterial host cells secreting the heavy chain a first Fd of an antibody that binds to a desired first antigen, wherein the first plurality of bacterial host cells contains DNA encoding the first Fd linked to a bacterial secretion signal peptide;

(b) introducing an antibody light chain fragment phage library encoding a plurality of different light chains, each linked to a bacterial secretion signal and a phage membrane anchor domain, into the first plurality of host cells of step (a) to cause secretion of phage libraries presenting two-chain ~~antibodies~~antibody fragments, each antibody fragment comprising the first Fd being composed of the heavy chain of step (a) and a light chain fragment;

(c) selecting a phage library that displays ~~antibodies~~antibody fragments that bind specifically to the ~~desired antigen of step (a)~~first antigen;

(d) introducing the phage library selected in step (c) into a second plurality of bacterial host cells secreting a second heavy chain that is the heavy chain Fd that is the Fd of an antibody that binds to a second desired antigen different from the first antigen, to create of step (a), to cause secretion of phage libraries presenting two-chain antibodies, each being composed of the second heavy chain antibody fragments, each comprising the second Fd and a light chain fragment, wherein the second plurality of bacterial host cells contains DNA encoding the second Fd linked to a bacterial secretion signal peptide; and

(e) selecting, from the phage libraries ~~secreted~~created in step (d), a phage library that displays two-chain ~~antibodies~~antibody fragments that bind specifically to the second desired antigen.

2. (Currently amended) A screening method comprising:

(a) providing a first plurality of bacterial host cells secreting the heavy chain of a first Fd of an antibody that binds to a desired first antigen, wherein the first plurality of bacterial host cells contains DNA encoding the first Fd linked to a bacterial secretion signal;

(b) introducing an antibody light chain fragment phage library encoding a plurality of different light chains, each linked to a bacterial secretion signal and a phage membrane anchor domain, into the first plurality of host cells of step (a) to cause secretion of phage libraries presenting two-chain ~~antibodies~~ antibody fragments, each antibody fragment comprising the first Fd being composed of the heavy chain of step (a) and a light chain fragment;

(c) selecting a phage library that displays ~~antibodies~~ antibody fragments that bind specifically to the ~~desired antigen of step (a)~~ first antigen;

(d) introducing the phage library selected in step (c) into a second plurality of bacterial host cells secreting a second heavy chain Fd comprising an amino acid sequence different from that of the heavy chain of step (a), to cause secretion of first Fd, to create phage libraries displaying two-chain ~~antibodies, each being composed of the second heavy chain antibody fragments, each antibody fragment comprising the second Fd and a light chain, wherein the second plurality of bacterial host cells contains DNA encoding the second Fd linked to a bacterial secretion signal;~~ and

(e) selecting, from the phage libraries ~~secreted~~ created in step (d), a phage library that displays antibodies that bind specifically to the ~~heavy~~ antigen recognized by the second ~~heavy chain Fd.~~

3. (Canceled)

4. (Previously Presented) The method of claim 1, wherein the host is *E. coli*.

5. (Previously presented) The method of claim 1, wherein steps (b) to (c) are carried out twice or more, with each subsequent round beginning with the phage library selected in step (c) of the prior round.

6. (Currently amended) The method of claim 1, wherein the method further comprises the following steps of:

(f) introducing the phage library selected in step (c) into a third plurality of bacterial host cells secreting a third heavy-chain that is the heavy-chain Fd that is the Fd of an antibody that binds to a third desired antigen different from the antigens of steps (a) and (d), to cause secretion of ~~create~~ phage libraries that display two-chain ~~antibodies, each being composed of antibody~~ fragments comprising the third heavy-chain Fd and a light chain fragment, wherein the third plurality of bacterial host cells contains DNA encoding the third Fd linked to a bacterial secretion signal; and

(g) selecting a phage library that displays two-chain ~~antibodies~~ antibody fragments that bind specifically to the third desired antigen.

7. (Currently amended) The method of claim 2, wherein the method further comprises the following steps of:

(f) introducing the phage library selected in step (c) into a third plurality of bacterial host cells secreting a third heavy-chain Fd comprising an amino acid sequence different from those of the heavy-chains of steps (a) and (d) first and second Fd's, to cause secretion of phage libraries that display two-chain antibodies, each being composed of the third ~~heavy-chain Fd~~ and a light chain fragment, wherein the third plurality of bacterial host cells contains DNA encoding the third Fd linked to a bacterial secretion signal; and

(g) selecting a phage library that displays ~~antibodies~~ antibody fragments that bind specifically to ~~the~~ an antigen recognized by the third ~~heavy-chain Fd~~.

8-9. (Cancelled)

10. (Withdrawn) A method for generating antibody light chains, wherein the method comprises the steps of:

- (a) selecting an antibody light chain from the screening method of claim 1;
- (b) generating a vector capable of expressing the selected light chain based on its genetic sequence;
- (c) introducing the vector into a host cell; and
- (d) culturing said host cell.

11-13. (Cancelled)

14. (Previously presented) The method of claim 2, wherein the host is *E. coli*.

15. (Previously presented) The method of claim 2, wherein steps (b) to (e) are carried out twice or more, with each subsequent round beginning with the phage library selected in step (e) of the prior round.

16-17. (Cancelled)

18. (Withdrawn) A method for generating antibody light chains, wherein the method comprises the steps of:

- (a) selecting an antibody light chain from the screening method of claim 2;
- (b) generating a vector capable of expressing the selected light chain based on its genetic sequence;
- (c) introducing the vector into a host cell; and
- (d) culturing said host cell.

19-26. (Canceled)

27. (New) A method of producing a multi-specific antibody fragment, the method comprising

(i) carrying out the screening method of claim 1 to select a phage library that displays two-chain antibody fragments that bind specifically to the second antigen;

(ii) selecting from the phage library of (i) a phage displaying a two-chain antibody fragment that binds to the second antigen and comprises the second Fd and a light chain fragment (the "selected light chain fragment");

(iii) producing a host cell comprising nucleic acid encoding (A) a light chain comprising the sequence of the selected light chain fragment, (B) a heavy chain comprising the sequence of the first Fd, and (C) a heavy chain comprising the sequence of the second Fd;

(iv) culturing the host cell of (iii) so that it expresses (A), (B), and (C) and assembles (A), (B) and (C) into a multispecific antibody comprising a copy of (B), a copy of (C), and two copies of (A), wherein (A) serves as a common light chain fragment for both (B) and (C).

28. (New) A method of producing a multi-specific antibody fragment, the method comprising

(i) carrying out the screening method of claim 2 to select a phage library that displays two-chain antibody fragments that bind specifically to the antigen recognized by the second Fd;

(ii) selecting from the phage library of (i) a phage displaying a two-chain antibody fragment that binds to the antigen recognized by the second Fd and comprises the second Fd and a light chain fragment (the "selected light chain fragment");

(iii) producing a host cell comprising nucleic acid encoding (A) a light chain comprising the sequence of the selected light chain fragment, (B) a heavy chain comprising the sequence of the first Fd, and (C) a heavy chain comprising the sequence of the second Fd;

(iv) culturing the host cell of (iii) so that it expresses (A), (B), and (C) and assembles (A), (B) and (C) into a multispecific antibody comprising a copy of (B), a copy of (C), and two copies of (A), wherein (A) serves as a common light chain fragment for both (B) and (C).

29. (New) The method of claim 27, wherein the host is *E. coli*.

30. (New) The method of claim 28, wherein the host is *E. coli*.

31. (New) A method of producing a multi-specific antibody fragment, the method comprising

(i) carrying out the screening method of claim 5 to ultimately select a phage library that displays two-chain antibody fragments that bind specifically to the second antigen;

(ii) selecting from the phage library of (i) a phage displaying a two-chain antibody fragment that binds to the second antigen and comprises the second Fd and a light chain fragment (the "selected light chain fragment");

(iii) producing a host cell comprising nucleic acid encoding (A) a light chain comprising the sequence of the selected light chain fragment, (B) a heavy chain comprising the sequence of the first Fd, and (C) a heavy chain comprising the sequence of the second Fd;

(iv) culturing the host cell of (iii) so that it expresses (A), (B), and (C) and assembles (A), (B) and (C) into a multispecific antibody comprising a copy of (B), a copy of (C), and two copies of (A), wherein (A) serves as a common light chain fragment for both (B) and (C).

32. (New) A method of producing a multi-specific antibody fragment, the method comprising

(i) carrying out the screening method of claim 7 to ultimately select a phage library that displays two-chain antibody fragments that bind specifically to the antigen recognized by the third Fd;

(ii) selecting from the phage library of (i) a phage displaying a two-chain antibody fragment that binds to the antigen recognized by the third Fd and comprises the third Fd and a light chain fragment (the "selected light chain fragment");

(iii) producing a host cell comprising nucleic acid encoding (A) a light chain comprising the sequence of the selected light chain fragment, (B) a heavy chain comprising the sequence of

the first Fd, (C) a heavy chain comprising the sequence of the second Fd, and (D) a heavy chain comprising the sequence of the third Fd;

(iv) culturing the host cell of (iii) so that it expresses (A), (B), (C), and (D) and assembles (A), (B), (C), and (D) into a multispecific antibody comprising a copy of (B), a copy of (C), a copy of (D), and three copies of (A), wherein (A) serves as a common light chain fragment for all of (B), (C), and (D).